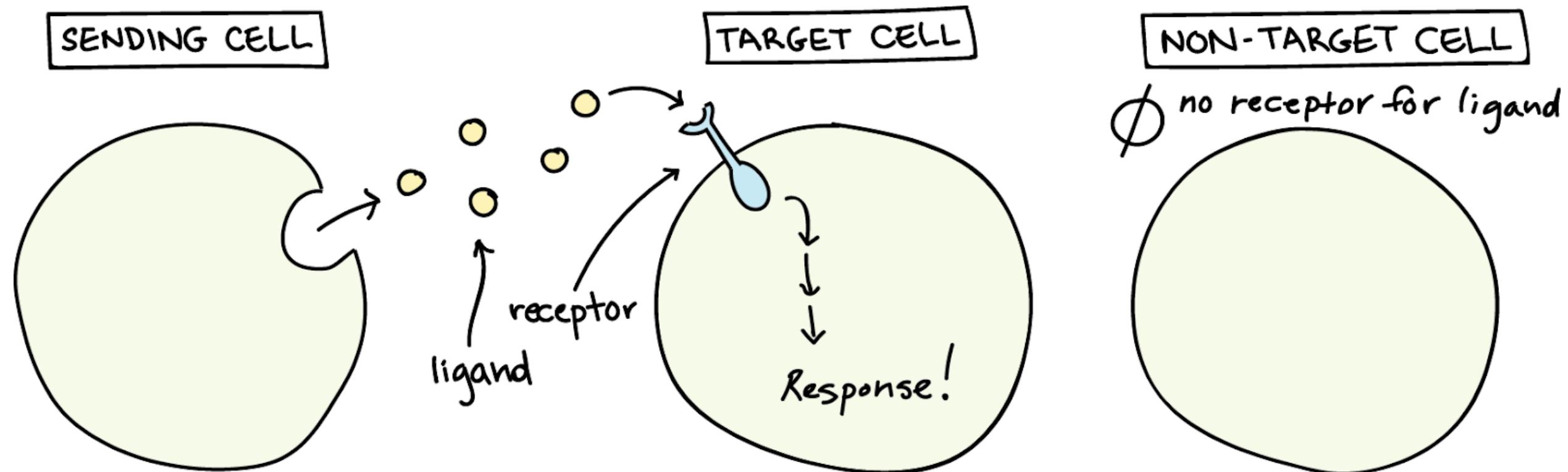


An Introduction to CellChat

Short Read Workshop, Day 8
Georgia Barone

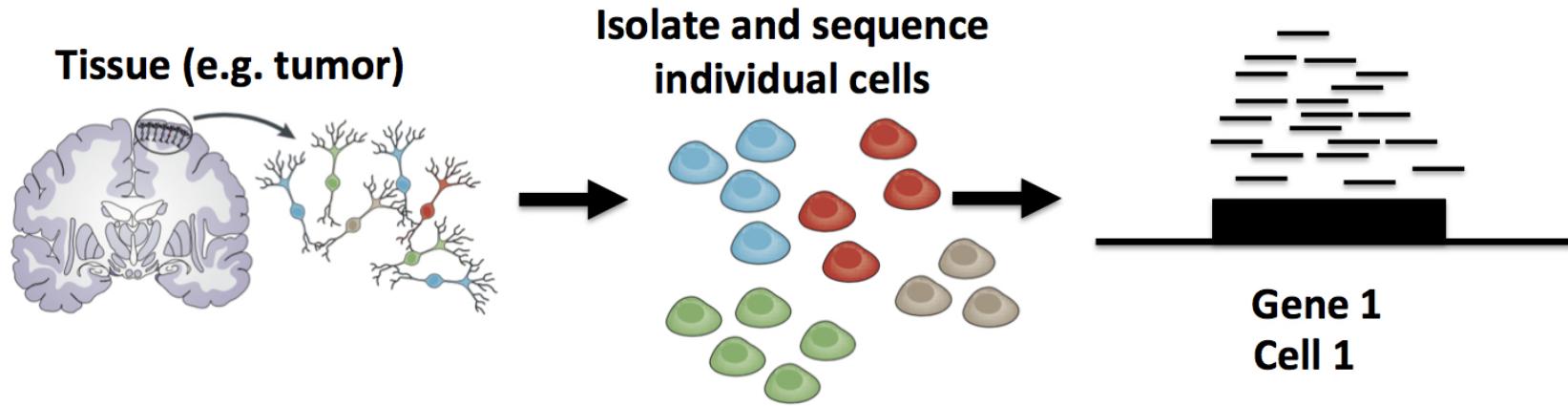
Cell-cell interactions coordinate cellular function



(Khan Academy)

CellChat leverages single-cell RNA sequencing data to evaluate cellular function

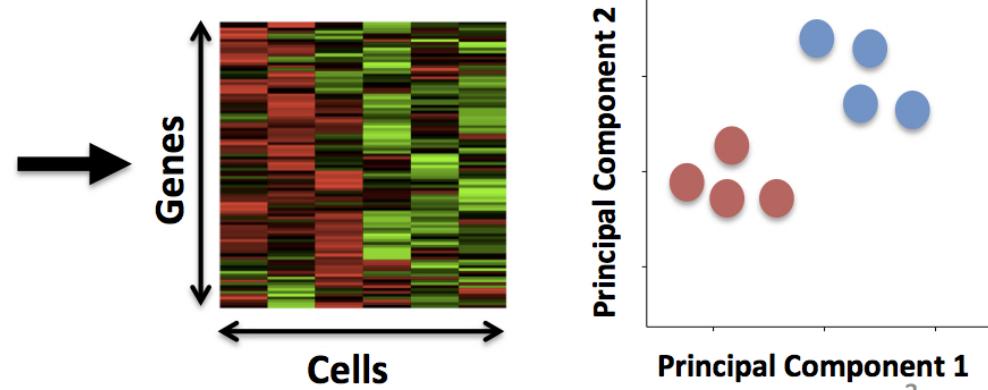
Input:
scRNA-seq



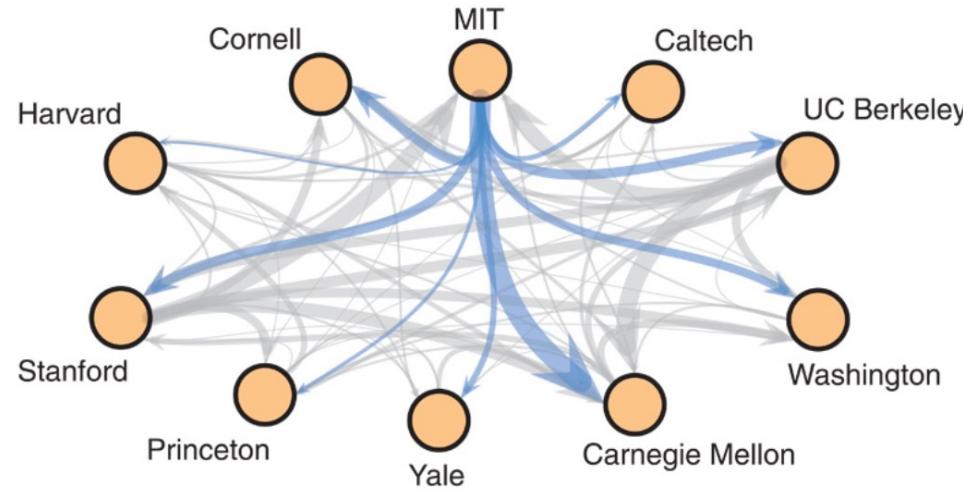
Read Counts

	Cell 1	Cell 2	...
Gene 1	18	0	
Gene 2	1010	506	
Gene 3	0	49	
Gene 4	22	0	
...			

Compare gene expression profiles of single cells



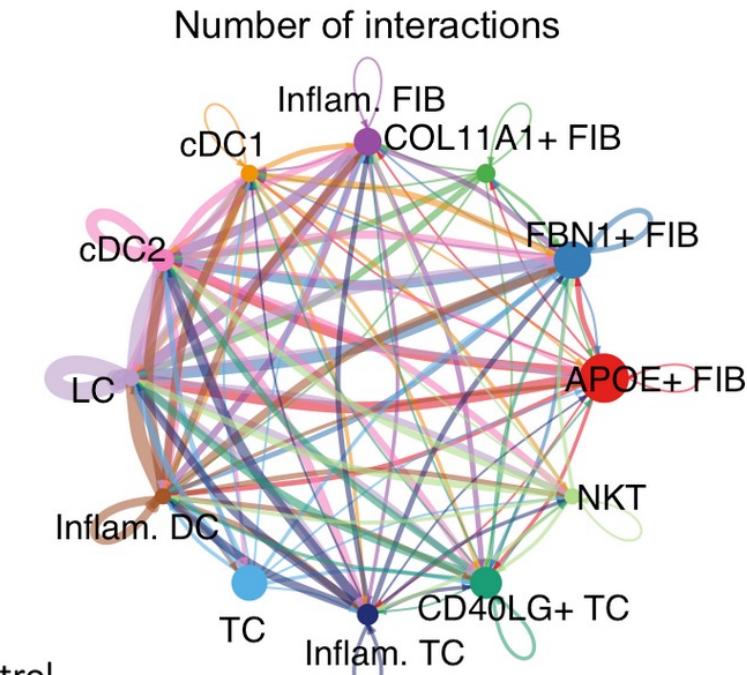
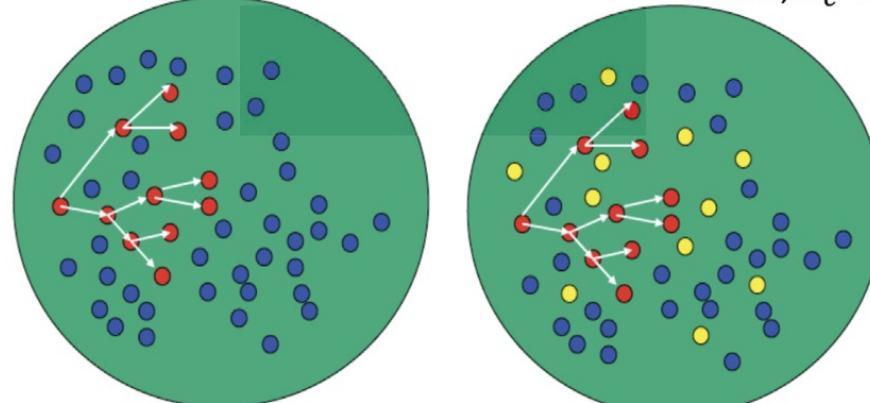
A network is a connected set of nodes and edges



Basic
reproduction
Number, $R_0=2$

- Susceptible individual
- Infectious individual
- Partially protected

Control
Reproduction
Number, $R_c=2$



(Larremore, 2015)
(Gumel, 2021)

CellChat utilizes a networks-based framework to model cell-cell communication

1. Cross reference a ligand-receptor interaction database

- Manually curated and validated signaling molecule interaction database (CellChatDB)

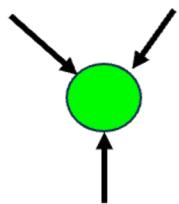
2. Inference and visualization of intercellular communications

- Identify differentially over expressed ligand-receptor pairs
- Build network (nodes = cell types; weighted edges = cell-cell communication probability)

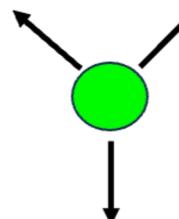
3. Quantitative Analysis

- Determine major signaling targets, sources, mediators, and influencers

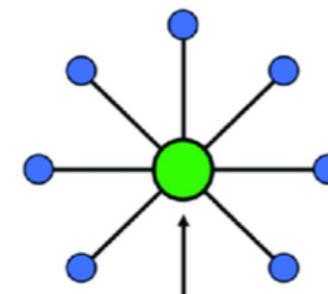
In-degree



Out-degree

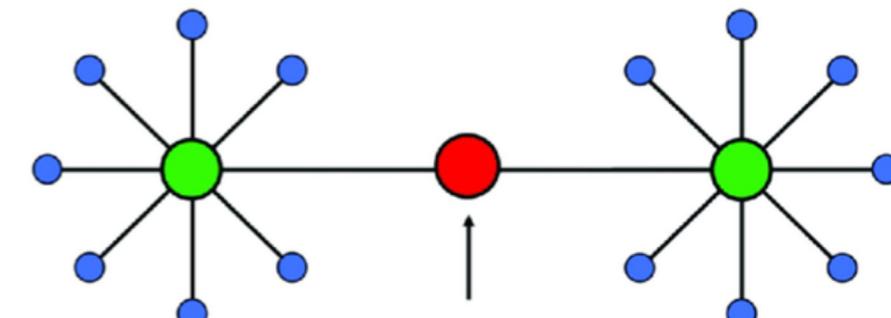


Degree Centrality



Highest Degree Centrality

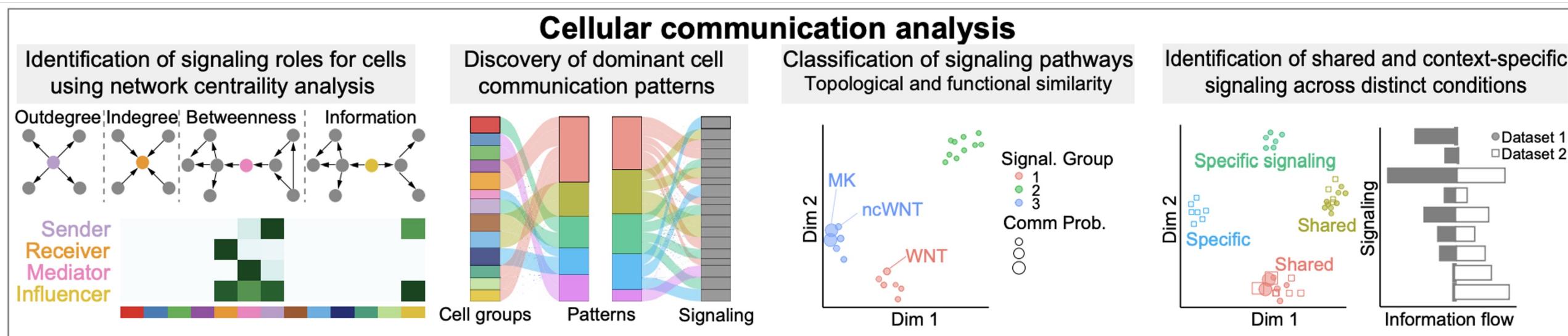
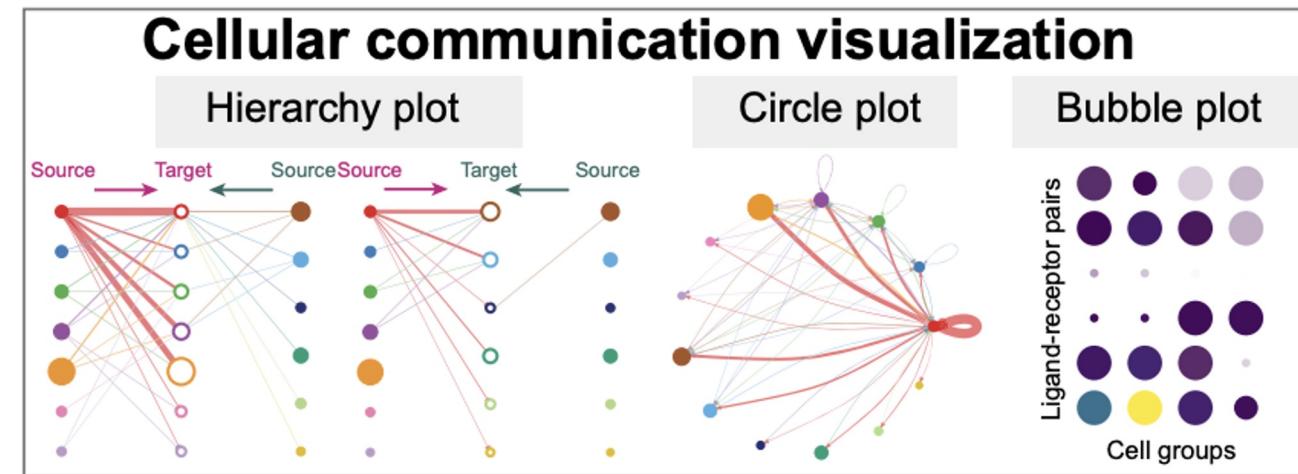
Betweenness Centrality



Highest Betweenness Centrality

CellChat utilizes a networks-based framework to model cell-cell communication

Output:



How to run CellChat

1. Load in Seurat object

poop

```
load("~/Desktop/short-read-scRNA/seurat-objs/t21_norm_seurat_obj.RData")
```

2. Convert Seurat object to CellChat object

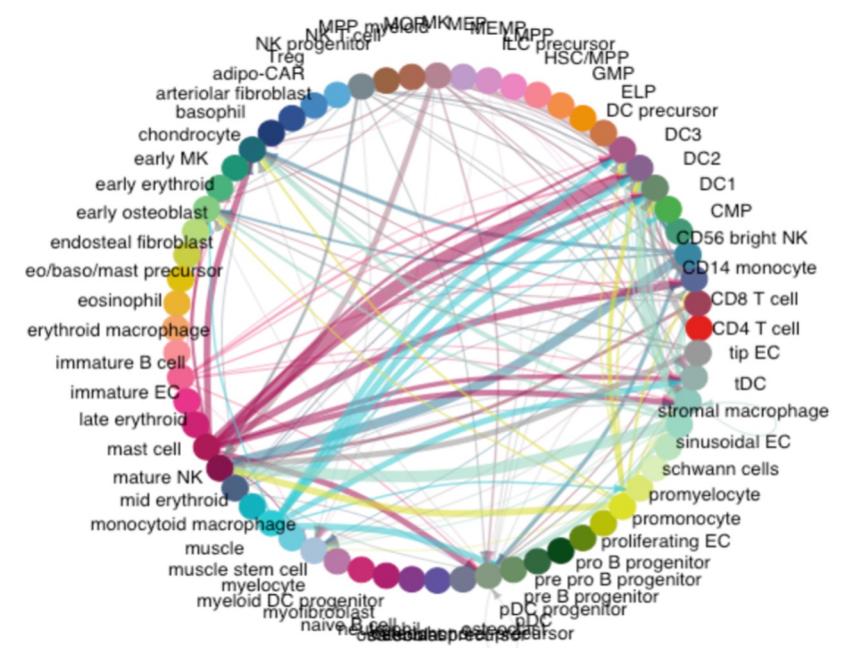
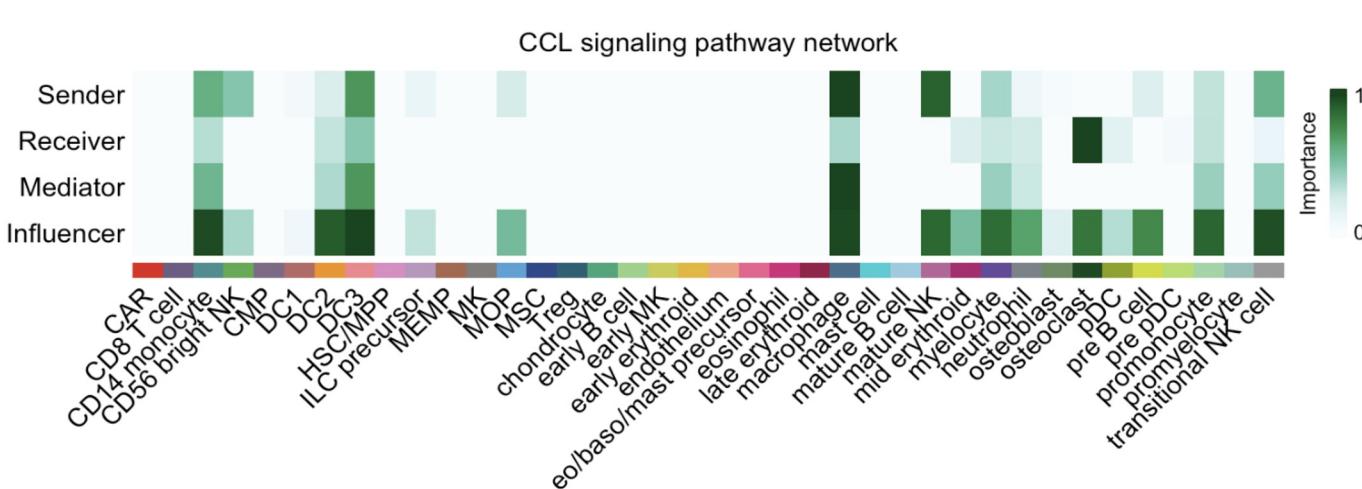
```
cellChat <- createCellChat(object = seurat_obj_t21, group.by = "cell.labels")
```

How to run CellChat

3. Calculate cell-cell communication probabilities

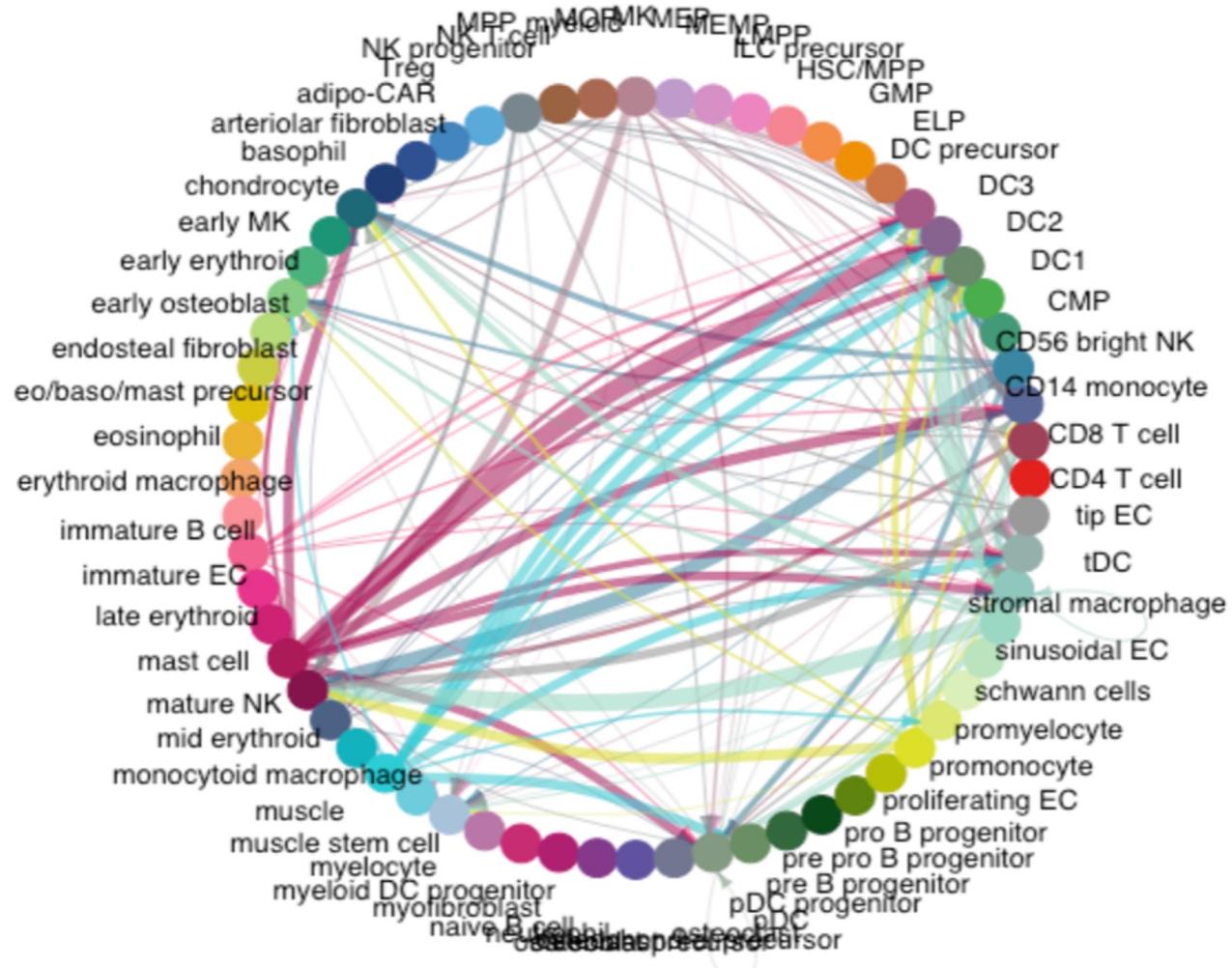
```
cellChat <- computeCommunProbPathway(cellChat)
```

4. Visualize results

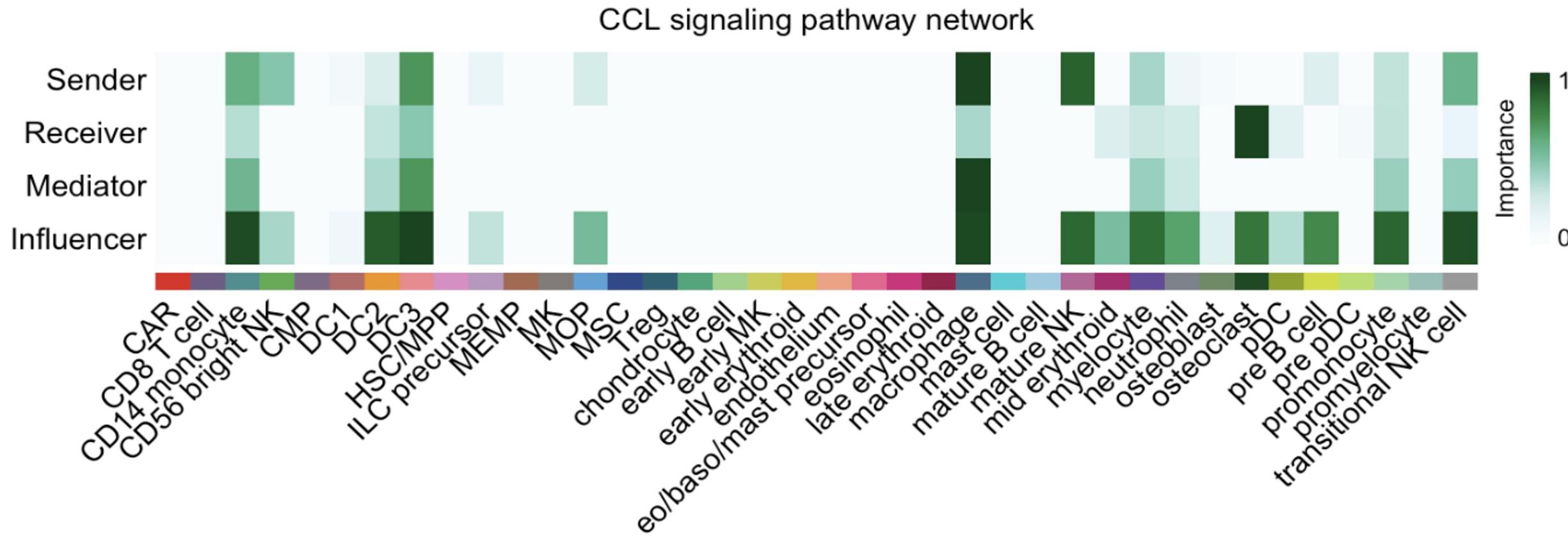


Example output:

CCL d21 signaling pathway network



Example output:



Work on Get-Started-With-CellChat.R

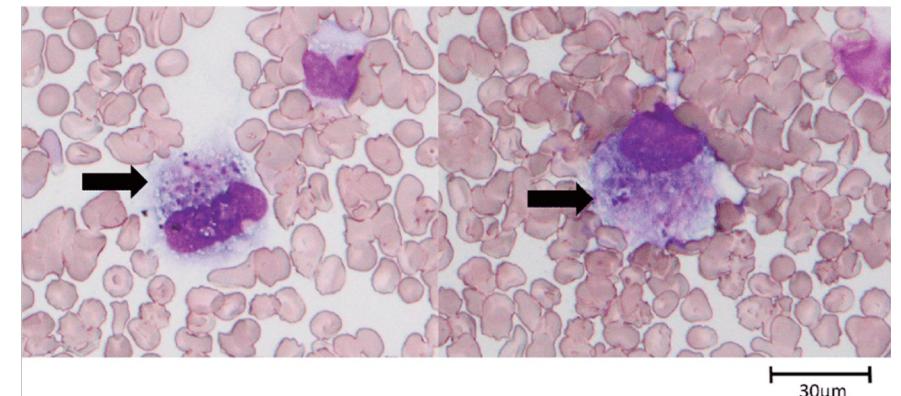
1. Run CellChat on a scRNA-seq data set from fetal bone marrow tissue of an individual with trisomy 21
2. If you finish early, run CellChat on another Seurat Object in the day9/. Look for interesting differences between the trisomic and disomic samples.

A Biological Conclusion...

Platelet concentration in T21 patients is lowered

While a heightened macrophage activity through the CCL pathway is crucial for making blood platelets it must be finely balanced

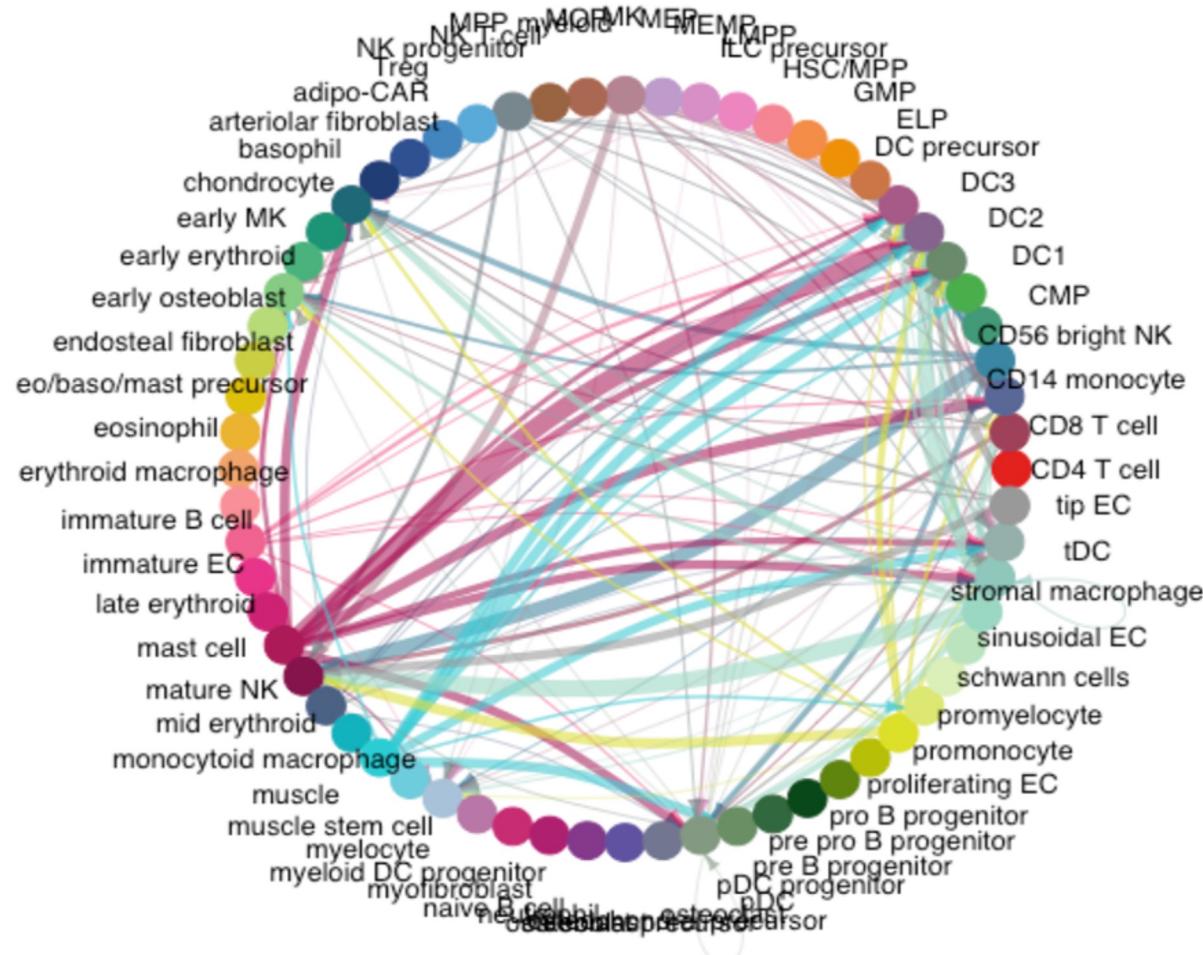
CCL dysregulation can lead to chronic inflammation, contributing to a range of chronic diseases and extra stress on the body



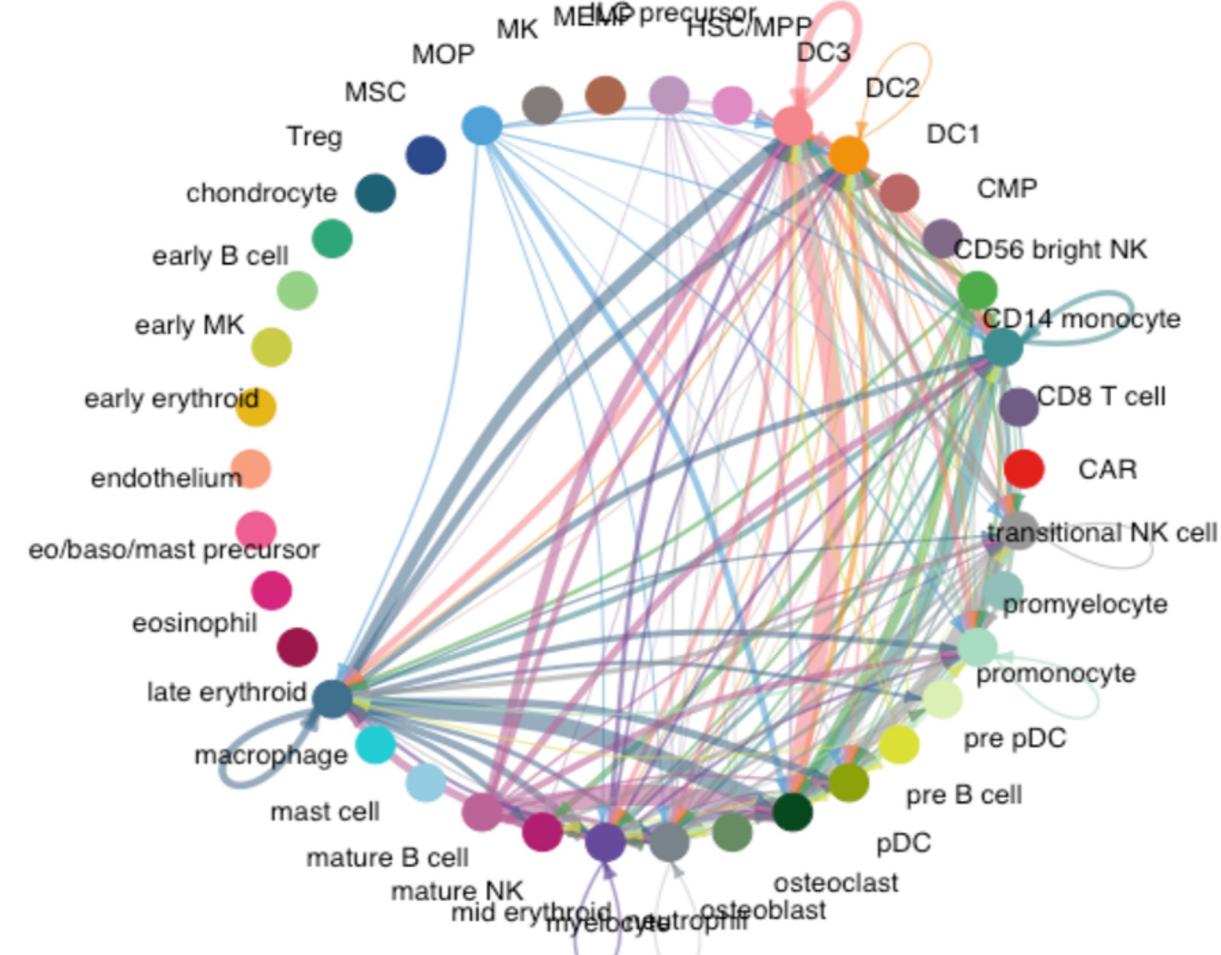
(Daisuke Hatanaka, 2022)

Cell-cell communication networks in the CCL pathway are altered in trisomy 21 fetus

CCL d21 signaling pathway network



CCL t21 signaling pathway network



Overall:

There are **more macrophage cells** in the **T21** fetus sending and receiving signals to other cells